Maternal and Child Health Journal, Vol. 7, No. 1, March 2003 (© 2003)

Commentary

Racial and Ethnic Disparities in Birth Outcomes: A Life-Course Perspective

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Background: In the United States, Black infants have significantly worse birth outcomes than do White infants. The cause of these persisting racial disparities remains unexplained. Most extant studies focus on differential exposures to protective and risk factors *during pregnancy*, such as current socioeconomic status, maternal risky behaviors, prenatal care, psychosocial stress, or perinatal infections. These risk factors during pregnancy, however, do not adequately account for the disparities. *Methods*: We conducted a literature review for longitudinal models of health disparities, and presented a synthesis of two leading models, using a life-course perspective. Traditional risk factors during pregnancy are then reexamined within their life-course context. We conclude with a discussion of the limitations and implications of the life-course perspective for future research, practice, and policy development. *Results*: Two leading longitudinal models of health disparities were identified and discussed. The early programming model posits that exposures in early life could influence future reproductive potential. The cumulative pathways model conceptualizes decline in reproductive health resulting from cumulative wear and tear to the body's allostatic systems. We propose a synthesis of these two models, using the life-course perspective. Disparities in birth outcomes are the consequences of differential developmental trajectories set forth by early life experiences and cumulative allostatic load over the life course. *Conclusions*: Future research on racial disparities in birth outcomes needs to examine differential exposures to risk and protective factors not only during pregnancy, but over the life course of women. Eliminating disparities requires interventions and policy development that are more longitudinally and contextually integrated than currently prevail.

KEY WORDS: racial–ethnic disparities; infant mortality; life course; early life programming; cumulative pathways; allostatic load.

BACKGROUND

Healthy People 2010 has identified eliminating health disparities as one of its two major goals for the decade (1). One of the most persisting health disparities is that of birth outcomes between African Americans and White Americans. An African American infant born today is still more than twice as likely to die within the 1st year of life as a White infant. A significant portion of this Black–White gap in infant mortality is attributable to the near twofold increase in low birth weight (LBW) and preterm births, and the near threefold increase in very low birth weight (VLBW) and very preterm births, among Black infants (2).

The cause of the persisting racial–ethnic disparities in birth outcomes remains largely unknown. Most extant studies focus on differential exposures to protective and risk factors *during pregnancy*, such as current socioeconomic status (SES), maternal risky behaviors, prenatal care, psychosocial stress, and perinatal infections. Such snapshots during pregnancy,

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1092-7875/03/0300-0013/0 © 2003 Plenum Publishing Corporation

however, tell us little about the life experiences of the women we are comparing. The purpose of our paper is to propose an alternative approach to examine racial–ethnic disparities in birth outcomes by using a more longitudinal and integrative perspective that accounts for women's health and development over their life course (3).

One popular explanation for the disparities invokes racial differences in SES, often measured *at the time of pregnancy* in terms of household income, occupational status, or parental educational attainment. African American women, on average, have lower SES than do non-Hispanic White women (4), and lower SES is associated with increased risk for infant mortality, LBW, and prematurity (2, 5). Conventional wisdom regards race as a proxy for SES, and SES factors, in turn, explain racial differences in birth outcomes. However, most studies that have controlled for differences in SES continue to find residual Black–White disparities in birth outcomes (6–8). In fact, high-SES African American women still have higher infant mortality than do low-SES, non-Hispanic White women (9). Moreover, SES factors appear to be associated with increased risk of infant mortality and LBW among White women but not among Black women (10–12). While it is possible that the residual disparities result from misclassification error, measurement error, aggregation bias, or some unmeasured aspect of SES (13), these studies suggest that differences in current SES cannot fully account for racial disparities in birth outcomes.

Another popular explanation holds risky behaviors *during pregnancy* responsible for the racial disparities. Maternal cigarette smoking is a prime example of a risky behavior because it is strongly associated with adverse outcomes such as intrauterine growth restriction and preterm delivery (14). However, several studies (15, 16) have found, albeit by self-report, that Black women are less likely to smoke cigarettes in pregnancy than are White women. Moreover, African American women who did not smoke cigarettes during pregnancy still had higher rates of infant mortality than non-Hispanic White women who did (17). Similarly, the reported prevalence of alcohol and drug use among pregnant Black women appears no greater than that among White women (9, 18, 19). While it is possible that studies may not have considered all risk behaviors, a few studies have concluded that the contributions of behavioral risk factors during pregnancy to racial disparities in birth outcomes appear to be modest (9, 20).

Similarly, delayed and inadequate utilization of *prenatal care* among Black women has been identified as an important risk factor for the excess infant mortality, LBW, and prematurity among Black infants. The expectation that increased access to and utilization of prenatal care will improve birth outcomes and reduce disparities has shaped our national policy for nearly two decades (21). However, the effectiveness of prenatal care for improving birth outcomes, particularly in preventing LBW and prematurity, has yet to be conclusively demonstrated (22). Several reviews concluded that there is little done during standard prenatal care today that could be expected to reduce LBW (23, 24), and the substantial increased utilization of early and adequate prenatal care over the past decade has not led to a significant decline in singleton LBW births for either Black or White women (25). Additionally, African American women who initiated prenatal care in the first trimester still had higher rates of infant mortality than did non-Hispanic, White women with late or no prenatal care (17).

Over the past decade, two risk factors have emerged as promising explanations for racial–ethnic disparities in birth outcomes: stress and infection. Maternal psychological stress, typically operationalized as stressful life events or perceived stress or anxiety *during pregnancy*, is associated with increased risk for LBW and preterm delivery (26, 29). Maternal stress can cause increased release of norepinephrine and cortisol, which then activates placental corticotropin-releasing hormone (CRH) gene expression, thereby precipitating the biological cascade leading to the onset of preterm labor (30). Hobel *et al.* found maternal plasma levels of CRH to be significantly elevated by midgestation in women who subsequently delivered preterm (31). They also found the increase in CRH to be related to the level of maternal stress. Stress can also alter immune function, leading to increased susceptibility to intra-amniotic infection or inflammation (32, 33). Additionally, stress may induce high-risk behaviors as means of coping with stress (34). However, African American women have not consistently reported higher levels of stress during pregnancy (20), and an association between increased maternal stress and adverse birth outcome has not been consistently demonstrated (35).

Evidence is also accumulating that infections *during pregnancy* may play a key role in the pathogenesis of preterm birth, particularly very preterm delivery (36). While researchers have recently focused on bacterial vaginosis (BV), several other infections, including asymptomatic bacteriuria, sexually transmitted

infections, and peridontal infections, have all been implicated. African American women have higher rates of many lower urogenital tract infections (37). They also have higher rates of amniotic infection, as evidenced by higher incidence of amniotic infection syndrome, severe histologic chorioamnionitis, maternal fever during labor, premature rupture of membranes, early and very early neonatal mortality from sepsis (37). Insofar as infections are associated with preterm delivery and poor perinatal outcomes, these studies suggest that infections may be responsible for a significant portion of racial disparities in birth outcomes. However, the cause of this increased susceptibility to infections among pregnant African American women remains largely unknown, and to date antibiotic treatment of infections (other than for asymptomatic bacteriuria) (38) during pregnancy has yielded modest or no benefits (39, 40).

Insofar as LBW and prematurity result from a complex interplay of biological, behavioral, psychological, and social factors, continued search for any single cause of racial disparities is likely to prove futile. This recognition has led researchers to propose models that examined multiple factors. One such model (41) examined the association of 46 risk factors mostly *during pregnancy* with birth weight. After controlling for these factors in the multivariable regression model, a residual Black–White difference in birth weight was still found. More important, these 46 risk factors explained less than 10% of the variance in birth weight. Several other models (20, 42, 43) that examined multiple risk factors during pregnancy have also failed to account for a larger portion of the variance in birth weight.

A comprehensive review of the strengths and limitations of these and other pregnancy risk factors is beyond the scope of this paper. We note their inadequacies not to reject their potential contributions, but to catalyze some rethinking about disparities in birth outcomes. Later we will revisit these risk factors in a different light. Our premise is that current understanding of the cause of the persisting disparities in birth outcomes remains limited, and further advancement may be limited by the prevailing approach to studying disparities. Presently birth outcomes are explained largely in terms of what happens *during pregnancy* (e.g., current SES, maternal cigarette smoking, prenatal care utilization, and stress or infections during pregnancy), and disparities in birth outcomes are explained by differential exposures to protective and risk factors *during pregnancy*. We contend that the disparities are the consequences of not only differential exposures during pregnancy but differential developmental trajectories over the life span, as we will explain later.

The aims of our paper are to 1) propose an alternative approach to examine racial–ethnic disparities in birth outcomes by using the life-course perspective; 2) reexamine pregnancy risk factors within their life-course context; 3) discuss the limitations of the current life-course model; and 4) explore the implications of the life-course perspective for future research, practice, and policy development.

METHODS

Recognizing the limitations of current research with its narrow focus on studying risk and protective factors *during pregnancy*, we conducted a literature review of existing longitudinal models of birth outcomes and health disparities. We searched computerized databases, using key words "life-course," "longitudinal," "race," "disparity," and "birth outcome." In the Results section, we will present a selected review of the evidence supporting the two leading models—early programming and cumulative pathway—by which differential experiences and exposures that happen early in life and accumulate throughout the life course may lead to disparities in birth outcomes. We will then present a synthesis of these two models, using the life-course perspective. In the Discussion section, we will first revisit the pregnancy risk factors briefly noted in the Background section, using the life-course perspective. As stated earlier, our purpose is not to reject the contributions of these risk factors to our understanding of disparities, but rather to recast them within the context of women's life-course experiences. Second, we will discuss several important limitations to the current life-course model. Lastly, we will conclude with an exploration of the implications of the life-course perspective for future research, practice, and policy development.

RESULTS

The suggestion that life-course factors may have important bearing on future birth outcome is not new. The possibility that maternal health prior to pregnancy might influence infant health was a conclusion of a birth cohort analysis of mortality in Great Britain carried out by Kermack *et al.* in the 1930s (44).

Since then a substantial body of evidence has accumulated linking maternal health development across the life course to her future pregnancy outcome. Two broad mechanisms have been postulated—the early programming and cumulative pathway mechanisms.

Early Programming Mechanism

Early programming mechanism suggests that exposures and experiences during particular sensitive developmental periods in early life may encode the functions of organs or systems that become manifest in health and disease later in life (45). Several studies have documented the influences of prenatal factors on lifelong chances of developing coronary heart disease (46), diabetes mellitus (47), and hypertension (48). The biological mechanisms by which in utero events may influence adult health have not been clearly elucidated. David Barker and his colleagues hypothesized that fetal undernutrition during middle or late gestation raises the risk of "adult-onset" diseases via suboptimal programming of blood pressure regulation, cholesterol metabolism, and glycemic control (45). Others have similarly demonstrated the long reach of childhood risk exposures on the development of adult chronic diseases (49, 50). Systematic differences in experiences and exposures, from conception onward, may thus become embedded in developmental biology and manifested later in life as socioeconomic gradients or racial–ethnic disparities in health.

If fetal programming can affect adult health, it follows that fetal programming may also affect future reproductive potential. For example, it has been shown in both animal and human studies that perinatal stress is associated with high stress reactivity that persists well into adulthood (51, 53), which may be related to feedback resistance as a result of decreased expression of glucocorticoid receptors in the brain (54). In humans, this programming may continue during infancy and early childhood (55). Infants of depressed mothers have shorter attention spans, less motivation to master new tasks, elevated resting heart rates and cortisol levels, and reduced electroencephalogram activity in the high functional context (56). The persistence of heart rate and cortisol changes suggest a reprogramming of the infant's basic autonomic rheostat that may persist into adulthood. Women who report a history of childhood sexual and physical abuse exhibit higher hypothalamic-pituitary-adrenal (HPA) reactivity than do controls, as demonstrated by higher adrenocorticotropin (ACTH) and cortisol responses to standardized psychosocial laboratory stressor (57). Exposure to stress hormones during sensitive periods of immune maturation in early infancy may also alter immune function, leading to increased susceptibility to infectious or inflammatory diseases later on in life (58). Hypothetically, maternal stress could prime the HPA axis and immune system of her developing fetus with stress hormones, leading to higher stress reactivity and immune-inflammatory dysregulation that could increase her female offspring's vulnerability to preterm labor and LBW later on in life.

We are aware of no human studies that provide direct evidence to support early programming of future reproductive potential. Similar to studies linking birth weight to chronic adult diseases, a large number of studies relating maternal birth weight to her future reproductive outcomes may be suggestive of early programming. Over 30 years ago, Ounsted *et al.* (59) observed a downward shift in the birth weight distribution of women who delivered a small-for-gestational-age infant, compared to that of women who delivered an appropriate-for-gestational-age infant. Subsequent research has found an approximately twofold increase in the risk of perinatal and infant mortality (60), LBW (61–64), and preterm birth (65) associated with low maternal birth weight, which has been observed for both African American and White women (60, 63, 64). While some researchers have interpreted these findings as indirect evidence supporting genetic transmission of LBW and prematurity, a nongenetic explanation for this intergenerational clustering of birth outcomes involves early programming of a woman's reproductive potential that is shared by siblings and possibly even across generations (66). Lumey (67) found decreased birth weights among the offsprings of women who were exposed in utero to the Dutch famine of 1944–45 during first and second trimesters, but not among those whose mothers were exposed in utero during the third trimester. This study, as well as studies on birth outcomes in twins (68), suggest that there may be critical periods during in utero development during which future reproductive potential becomes encoded.

Cumulative Pathway Mechanism

Alternatively, the cumulative pathway mechanism posits how wear and tear can add up over time to affect health and function. Several studies have related health disparities to cumulative

differential exposures to damaging physical and social environments at different life stages (69, 70). The biological mechanisms by which disadvantages and inequities carried over a life course of differential exposures lead to health disparities are not well understood. It has been proposed that chronic accommodation to stress results in wear and tear, what Bruce McEwen refers to as "allostatic load" (71), on the body's adaptive systems. Studies (72, 73) have found in animals and humans subjected to chronic and repeated stress elevated basal cortisol levels and exaggerated ACTH and cortisol responses to natural or experimental stressors. This HPA hyperactivity may reflect the inability of a worn-out HPA axis for self-regulation, possibly due to the loss of feedback inhibition via downregulation of glucocorticoid receptors in the brain (72). Similarly, chronically elevated levels of cortisol may also lead to not only relative immune suppression, but also immune-inflammatory dysregulation because of the loss of counterregulation by the HPA axis, resulting in part from downregulation of glucocorticoid receptors in the immune cells (74). HPA hyperactivity and immune-inflammatory dysregulation are two of several possible mechanisms by which chronic and repeated stress over the life course may lead to increased risk for cardiovascular diseases, cancers, autoimmune disorders, and a host of chronic adult diseases that contribute to health disparities.

It follows that allostatic load over the life course should also affect reproductive health. Women who are subjected to chronic and repeated stress may respond to stressors during pregnancy with higher output of norepinephrine and cortisol, which could increase CRH gene expression leading to preterm labor. Higher levels of glucocorticoids can also lead to relative immune suppression, which could increase the likelihood of chronic colonization of the genital tract by pathogens at conception and during early pregnancy. If they are not cleared by midgestation, spontaneous preterm labor or preterm premature rupture of membranes may follow (36). Alternatively, chronically elevated levels of glucocorticoids can result in loss of HPA counterregulation of the body's immune-inflammatory response. In response to an infection, even one as innocuous as BV, excessive amount of proinflammatory mediators is released, which could precipitate preterm labor. One recent study found that women with previous early preterm deliveries who had evidence of intra-amniotic infection or inflammation had significantly higher tumor necrosis factor alpha production after stimulation by lipopolysaccharide, compared with women with previous term deliveries, even 5 years out from their previous delivery (75). Thus vulnerability to preterm delivery may be traced to not only stress and infection during pregnancy, but more important HPA hyperactivity and immune-inflammatory dysregulation that may have been patterned by lifelong exposures to chronic and repeated stress.

Evidence supporting the cumulative pathway mechanism comes from research on the weathering hypothesis. Geronimus (76) found a fourfold increase in the risk of LBW and VLBW births with increasing age among African American women but not among White women. Moreover, among African American women the elevated risk with increasing age was seen only in women of low and average SES, but not in those of high SES. She also noted a more rapid decline in the health status of African American women than that of White women with increasing age, particularly among the disadvantaged. Geronimus attributed the accelerated decline in the health status of disadvantaged African American women with increasing age to the chronic stress and strain that they have to weather day in and day out throughout their life course. The cumulative impact of the allostatic load on their reproductive health is manifested in the increasing rates of LBW and VLBW births with increasing age. Stein *et al.* (77) found among a large cohort of homeless women that the percentage of life one had spent being homeless had a stronger association with LBW and preterm delivery than whether or not one was homeless during the index pregnancy. This lends further support to the weathering hypothesis that what a woman has weathered through prior to pregnancy, and what she bring to bear on it, may have equal, if not greater, impact on the outcome of the pregnancy than what happens during it.

The Life-Course Perspective—A Synthesis

The early programming model and the cumulative pathways model are not mutually exclusive. The early programming model emphasizes the importance of sensitive developmental periods in utero or early life during which future reproductive potential becomes programmed. However, it does not adequately address the processes of development and decline beyond early life. In contrast, the cumulative pathways model conceptualizes a more gradual decline in reproductive potential resulting from cumulative wear and tear to the body's allostatic systems over the life course, but it does not adequately acknowledge the importance of critical or sensitive periods. We posit

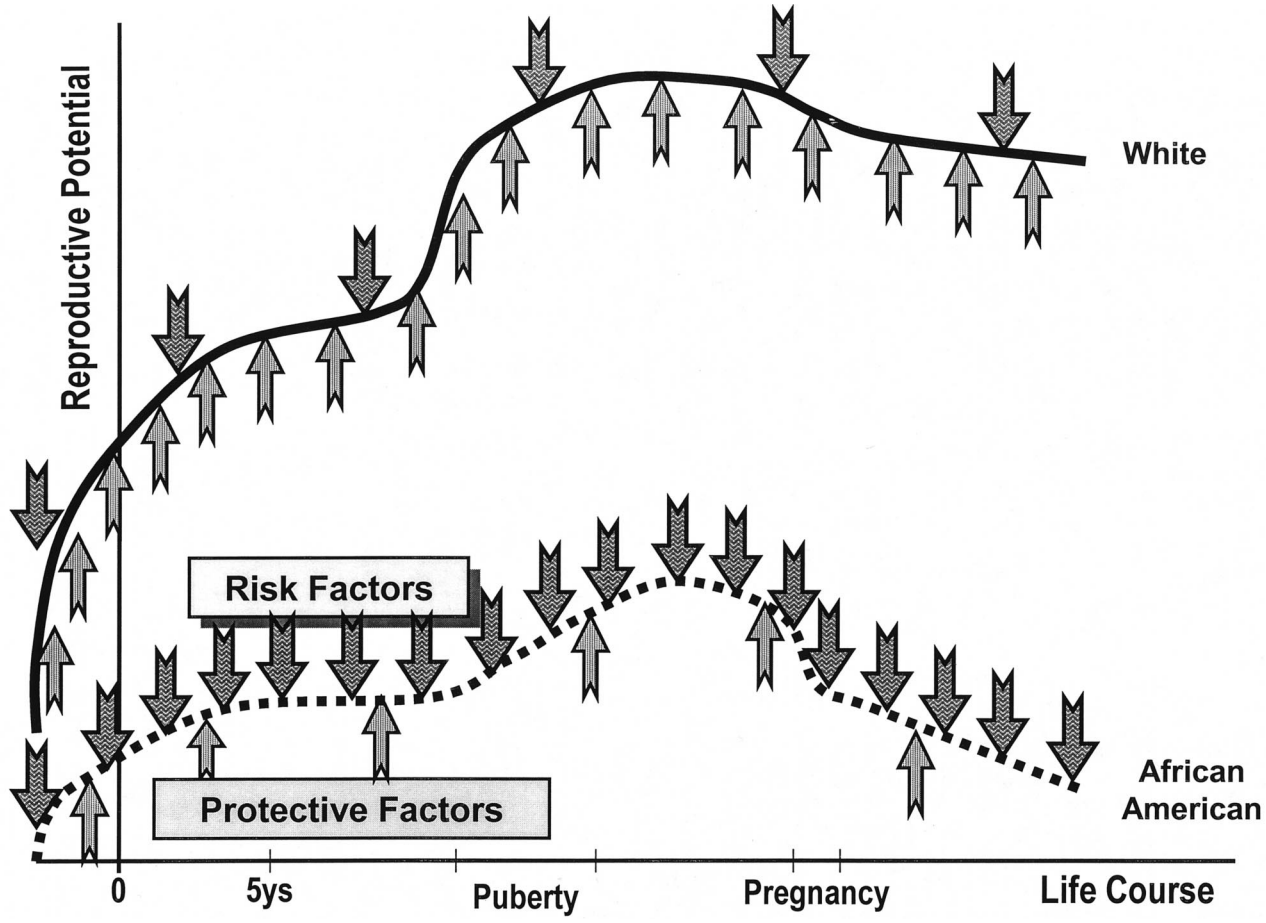

Fig. 1. How differential exposures to risk factors (downward arrows) and protective factors (upward arrows) over the life course affect developmental trajectories and contribute to disparities in birth outcomes. The lower reproductive potential of African American women, relative to White women, results from their cumulative exposure to more risk factors and less protective factors across the life span, particularly during sensitive periods of development.

that both mechanisms are at play in shaping health trajectories over the life course.

We propose a life-course health development model which integrates these two complementary mechanisms to explain how different health trajectories develop (3). This model synthesizes both the programming mechanisms of early life events and the cumulative pathway mechanisms of allostatic load over the life course into a longitudinal model of health development, as diagrammed in Fig. 1. The x-axis depicts age across the life span, and the y-axis represents the function of a tissue, organ, or system, such as cognitive capacity or pulmonary function. Thus a woman's reproductive potential is viewed as the product of her developmental trajectory over the life course. The trajectory is drawn as curves rather than as straight lines to underscore the notion of sensitive periods during which development is particularly vulnerable to the influences of "risk factors" (downward arrows) and amenable to those of "protective factors" (upward arrows). These sensitive periods are depicted in Fig. 1 as steep accelerations in the slopes of the developmental trajectory that occur in utero and early life and possibly during puberty, although we caution that the depiction is necessarily conjectural at present since the timing of these sensitive periods and the effect of particular influences on reproductive potential have not been clearly elucidated.

The trajectory is also drawn to account for the processes of development and decline outside of these sensitive developmental periods. The slopes of the trajectory at different life stages are determined by the balance of the number of upward arrows that "push up" and downward arrows that "push down" on the

trajectory. While presently it is not clear at what stage the trajectory peaks, the downward slope following the peak represents in part the decline in reproductive potential resulting from cumulative wear and tear on the body's allostatic systems. The depiction of a more rapid deceleration in the slope of the trajectory during pregnancy is also conjectural at present, suggesting pregnancy as a particularly vulnerable period. Thus a woman's reproductive potential is a function of her developmental trajectory set forth by early life experiences (early programming mechanism) and altered by cumulative allostatic load (cumulative pathways mechanism) over the life course (Fig. 1).

We propose using this life-course perspective to reexamine racial–ethnic disparities in birth outcomes. The life-course perspective reconceptualizes determinants of birth outcomes longitudinally as part of the developmental process for reproductive health; it provides a longitudinal account of the interplay of biological, behavioral, psychological, and social protective and risk factors in producing adverse birth outcomes. Disparities in birth outcomes result from differential developmental trajectories over the life course, as depicted in Fig. 1. These trajectories are drawn to start at different points on the y-axis to account for possible intergenerational effects. The Black–White gap in reproductive potential widens in utero and early life, and possibly during puberty, pregnancy, and other sensitive periods of development. Outside of these sensitive periods, the gap continues to widen as a result of differential cumulative exposures to protective and risk factors. Thus the lower reproductive potential of African American women, relative to White women, results from 1) lower starting point due to intergenerational effect, 2) smaller acceleration and greater deceleration in their developmental trajectory during sensitive periods, and/or 3) exposures to more risk factors (downward arrows) and less protective factors (upward arrows) across their life span.

From the life-course perspective, eliminating racial–ethnic disparities in birth outcomes will require 1) closing the gap in one generation to give the next generation an equal start, 2) targeted interventions during sensitive developmental periods (e.g., in utero development, early childhood, puberty, pregnancy), and 3) risk reduction and health promotion strategies across the life span, as illustrated in Fig. 2. Such strategies "pull up" the trajectory by mitigating risk factors, and "push up" the trajectory by promoting protective factors. It should be evident from Fig. 2 that closing the gap between Black and White curves will require risk reduction and health promotion strategies to be not only applied during pregnancy, but sustained over the life course, particularly during sensitive periods of development (Fig. 2).

DISCUSSION

We will now 1) revisit the aforementioned pregnancy risk factors; 2) discuss the limitations of the current life-course model; and 3) explore the implications of the life-course perspective for future research, practice, and policy development.

Pregnancy Risk Factors Revisited

The life-course perspective allows us to recast pregnancy risk factors (e.g., SES, behaviors, prenatal care, stress, and infections) in the context of women's life-course health development. The impact of race on birth outcomes can also be better understood within this life-course context. We contend that these risk factors exert their influence over birth outcomes not only during pregnancy, but from early life and across women's life span. We further contend that the life-course context of these risk factors differ between Black and White women, resulting in differential impact on their reproductive health.

Socioeconomic Status

The life-course perspective suggests that past SES may be as important a determinant of birth outcomes as current SES. This suggestion does not reject the contributions of current SES; instead it posits that the residual disparities after controlling for current SES may be partially attributable to unmeasured effects of past SES. Studies by investigators in Aberdeen, Scotland, in the 1950s found that women who were born into a lower social class had lower rates of perinatal mortality and LBW if they married into a higher social class than if they married within the lower social class (78). But these so-called "upwardly mobile" women still had higher rates of adverse pregnancy outcomes than did women who were born into a higher social class (78). These studies indicate that both the conditions under which a mother is born and grows up and the conditions under which her pregnancies occur are both important determinants of her reproductive success. They also suggest that it may take more than one generation to equalize socioeconomic disparities in birth outcomes (79). This may explain in part the persisting gap in birth outcomes

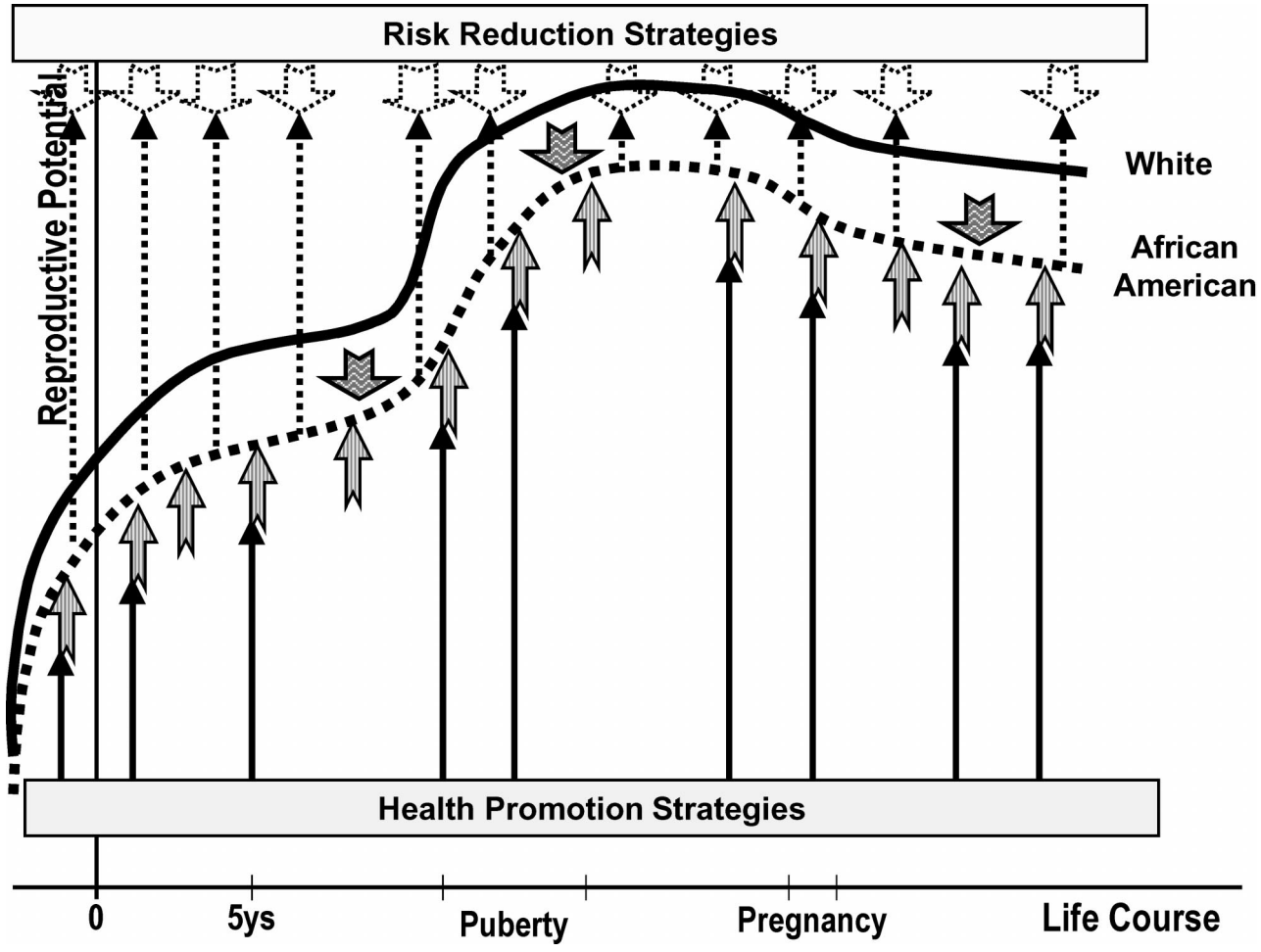

Fig. 2. How interventions throughout the life course, and particularly during sensitive periods of development, such as risk reduction strategies (dashed lines) and health promotion strategies (solid lines), might change developmental trajectories and close the Black–White gap in reproductive potentials.

among African American women of high SES, since most had attained their status only within the past generation (80).

However, the findings of higher risk for LBW and prematurity among high-SES African Americans even after two generations of affluence (81) suggest that high SES may not provide the same level of protection for African American women as it does for White women. Several studies have shown that the decrease in LBW with increasing maternal SES was much smaller among African American women than the decrease among White women (10–12). Within the same SES category, African American women may be exposed to more risk factors and less protective factors over their life course than may be their White counterparts. They may experience more discrimination, and may be exposed to more social stressors. One study (82) reported that many middle-class Black women are willing to live under conditions of systematic neglect in exchange for the protective features of living in a Black community, including more limited exposure to racism in their neighborhoods. Presumably middle-class White women do not have to make this trade-off of one set of stressors for another. Middle-class Black women may also be more concerned about the fragility of their social status, and may thus be more vulnerable to the detrimental effects of John Henryism on health (82). Compared to White families with similar incomes, middle-class Black families have only a third of their wealth or net worth. In sum, the same SES may mean very different life histories for Black and White women.

Thus to better understand the contributions of SES to racial disparities in birth outcomes, researchers need to examine racial differences in not only current SES, but also past SES and the life-course context of SES.

Behaviors

Although a few studies have suggested that the contributions of behavioral risk factors *during pregnancy* to disparities in birth outcomes appear to be modest, much less is known about those of behavioral risk factors *before pregnancy* and *over the life course*. Little is known, for example, about the effects of preconceptional smoking or pubertal poor nutrition on birth weight. The life-course perspective posits that past behaviors, particularly during periods of risk, may affect future reproductive success to a similar, if not greater, extent as current behaviors. It also views risk behaviors during pregnancy in continuum with risk behaviors throughout the life course. Most risk behaviors do not arise de novo during pregnancy, and their cumulative impact may persist even if the behaviors cease during pregnancy. While it is generally accepted that pregnancy provides a window of opportunity for behavioral modifications, many prenatal interventions may have greater impact on improving birth outcomes if they begin preconceptionally.

The same risk behaviors may have differential impact on the birth outcomes of Black and White women. For example, cigarette smoking appears to be more virulent among Black women than among White women (10). The cause of this higher virulence is not known, but may be related to the interaction of cigarette smoking with other life-course factors that are more prevalent among Black women. For example, cigarette smoking could interact with psychosocial stress to produce a multiplicative effect on vascular dysfunction and immune-inflammatory dysregulation in the placenta (83), leading to increased risk for IUGR and preterm delivery. Black women may be more vulnerable to the interactive effects of smoking and stress because of their increased exposures to life-course stressors. Disparities are likely the result of complex interactions among multiple factors at multiple levels across the life-course rather than single behavioral risk factors during pregnancy. As Hogan *et al.* (84) observe, it is no longer valid to look solely at one risk factor at a time without taking on the additional scientific task of understanding the role interactions play.

Prenatal Care

From the life-course perspective, it is perhaps not surprising that prenatal care (22–24), or even enhanced prenatal care (85), has not been conclusively demonstrated to be effective in preventing LBW and prematurity. To expect prenatal care, in less than 9 months, to reverse the impact of early life programming and cumulative allostatic load on women's reproductive health, may be expecting too much of prenatal care. This may explain why African American women who initiated prenatal care in the first trimester still have higher rates of infant mortality than do non-Hispanic, White women with late or no prenatal care (17). Prenatal care as currently prevails may do too little too late to have a major impact on disparities in birth outcomes. Even preconceptional care may do too little too late if it is provided in a single visit shortly before a planned pregnancy, rather than as an integral part of women's health care continuum for all women of reproductive age (86).

Prenatal care may also have differential impact for Black and White women. Several studies (87–88) suggest that prenatal care may be more beneficial for Blacks than for Whites, although these studies may not have adequately controlled for selection bias on the part of Black women who obtain early and adequate prenatal care. The opposite may be true in light of the findings by Kogan *et al.* (89) that Black women may be at greater risk for not receiving information from their prenatal care providers that could reduce their chance of an adverse pregnancy outcome. They are also less likely to receive a pelvic examination, blood or urine test, and blood pressure check during their prenatal care visits (26). They receive less ultrasound, amniocentesis, and tocolytic treatment than do White women (90). Thus the same level of utilization may not indicate the same content or quality of care for Black and White women.

Stress

Much of current research on stress and birth outcomes has focused on acute, individual psychological stressors that occurred immediately before or during pregnancy (e.g., Stressful Life Events). Even measures of chronic stress (e.g., Perceived Stress Scale) assess the degree to which the pregnant woman appraises her situations as stressful only during the

past month. Anxiety is often measured as generalized anxiety within the past 7 days (Spielberger State Anxiety Scale), or as related to the health of the baby or fear of the labor and delivery process (Pregnancy Anxiety Scale). Perhaps it is not surprising that pregnant African American women have not consistently scored higher on these scales than have White women (20), or that an association between these measures of stress and anxiety during pregnancy and adverse birth outcome has not been consistently demonstrated (35). These measures do not fully capture the chronic social stressors that are pervasive in the everyday lives of many African American women (84). We contend that it is these stressors (e.g., factors in the community, social relationships, economics, discrimination, politics, housing, etc.) that over time cause wear and tear on the body's allostatic systems, and that underlie racial disparities in birth and other health outcomes. The disappointing results of many intervention programs that aim at improving birth outcomes by providing psychosocial support to pregnant women may be partially attributable to their failure to address these chronic social stressors (91).

As discussed earlier, differential exposures to life-course stressors can pattern different stress response. One experiment found that African American women responded to subtle unfair treatment with greater cardiovascular reactivity than did White women (92). Among African American women, those who attributed the mistreatment to racial discrimination exhibited even greater cardiovascular reactivity. Thus the same experimental stressor can elicit different stress appraisal and response in Black and White women. The cause of this racial difference in stress reactivity is not clear, but may be related to differential exposures to allostatic load over the life course. We hypothesize that the higher rate of preterm delivery among African American women is related to not only stress exposures during pregnancy, but more important stress response that has been patterned by lifelong exposures to chronic and repeated stress. Thus to better understand disparities in birth outcomes, it may not be sufficient to study stressors during pregnancy; researchers need to examine the dynamic between life-course stressors and patterned stress response in creating differential vulnerabilities to stress during pregnancy.

Infection

As discussed earlier, the infection responsible for preterm delivery may already be present in the urogenital tract in early pregnancy or even before conception (36). Perhaps this explains the disappointing results of most antibiotic trials in pregnancy. Screening for and treating an infection with antibiotics weeks or even months after its onset may prove to be ineffective. Even if the infection is treated, it may be too late to arrest the immune-inflammatory processes that have long been initiated, particularly if the host is unable to modulate the amount of immune-inflammatory response. While a great deal of attention in research over the past decade has focused on identifying and treating infectious pathogens that may be responsible for preterm delivery, much less is known about the contributions of host immunity. The findings of spontaneous resolution of BV in a substantial proportion of women who received placebo (40, 93), and of differential treatment efficacy by risk status in several trials (93, 94) suggest a role for host immunity. While the higher rates of urogenital tract and other infections among pregnant African American women have been well documented, we are aware of no studies that have explored racial differences in host resistance to infections in pregnancy.

Even less is known about the contributions of environmental conditions to host resistance during pregnancy (95). Are there elements in the physical and social environments of pregnant African American women that increase their susceptibility to infections? Culhane *et al.* (96) found high levels of chronic stress during pregnancy to be associated with BV, independent of the effects of other established sociodemographic and behavioral risk factors for BV. Do the chronic social stressors that are pervasive in the lives of African American women play a role in their higher risk for BV? To date there has been only one study (97) linking stress to immunity in human pregnancy using superficial immune measures, and we are aware of no studies that have examined the interplay between psychosocial stress and host immunity in the context of racial disparities. Thus while studying infections during pregnancy appears promising, future research needs to examine the interactions between host immunity and environmental factors in creating differential vulnerabilities to infections during pregnancy.

Race and Racism

We now revisit race as a risk factor. Over the past several decades, genetic explanations have largely been rejected on the basis of the argument that race

and ethnicity are socially delimited constructs rather than biologically defined categories; human genetic diversity appears to be a continuum, with no clear breaks delineating racial groups (98). While there are clearly racial differences in genetic susceptibility to certain diseases (e.g., sickle cell disease), the role that specific genes play in several of the birth outcomes that contribute significantly to racial and ethnic disparities, such as LBW or prematurity, is less clear. Recently Wang *et al.* identified two genes, *CYP1A1* and *GSTT1*, to be associated with LBW and shortened gestation, but only among carriers who were exposed to certain environmental toxins, such as benzene (99) and cigarette smoking (100). Genetic susceptibility alone did not confer a higher risk for LBW or prematurity among nonexposed carriers. Their finding of a significant interaction effect on birth weight between maternal smoking and *CYP1A1* and *GSTT1* genotypes among African American but not White women has renewed interests in reexamining genetic contributions to racial disparities, not in terms of nature versus nurture, but of gene-environment interactions. Meaney *et al.* (101) have demonstrated in rat models that gene expression for glucocorticoid receptors in the hippocampus and frontal cortex can be altered by early life stressors, resulting in increased HPA reactivity to stressful stimuli that persist throughout the life of the animal. This raises the possibility that gene-environment interactions may also play a role in stress-mediated health outcomes, including LBW and preterm delivery. Future research should explore racial differences in not only genetic susceptibility (e.g., distribution of gene polymorphisms), but more important multiple gene-environment interactions in producing health disparities.

While race as a biological concept may have little scientific meaning, as a social construct it may have profound health consequences (102). Several studies have found an association between self-reported experiences of racial discrimination and impaired health (103). A recent case-control study found that among low-income African American women in Chicago, the adjusted odds of giving birth to a VLBW infant were 3.3 times greater among women who reported having experienced racial discrimination than among those who did not (104). Racism can take multiple forms; it can be internalized, personally mediated, or institutionalized (105). It can manifest itself as discriminatory medical care. Several studies have documented that African Americans receive less ambulatory, hospital, and disease-specific care than do Whites and experience greater barriers in their interactions with the medical care system (106). It can also manifest itself in residential segregation. Greater Black–White gap in infant mortality has been found in cities that are more segregated (107, 108). Exposure to racial discrimination is not limited to pregnancy, but extends across the life span. The effect of race on birth outcome is likely mediated in part through this weathering of racism and racial discrimination over the life course.

Limitations of the Current Life-Course Model

There are several important limitations to the current life-course model. First, the life-course literature is still in its early gestation. Biological evidence from animal studies needs to be interpreted with caution in the human context. For example, while numerous animal studies on the life-course development of stress reactivity and immune function have provided intriguing data on how social inequality may cause health disparities (72), their relevance to the human context is at best speculative. Epidemiological data from most human studies are associational in nature and do not elucidate biological pathways. We are not aware of any human studies that have demonstrated population differences in stress reactivity and immune function among pregnant women, nor have there been studies linking these differences to social inequality over the life course. Future life course studies need to better integrate biomedical and social–behavioral research on disparities.

Second, existing life-course factors still tell little of women's life history. Thus it is not surprising that these so-called "life-course factors," such as maternal birth weight or maternal grandfather's occupation, also appear to explain only a small portion of the variance in birth outcomes. Future life-course research needs to develop instruments which measure more accurately, precisely, and inclusively "life-course" risk factors (109). For example, stress should be measured not simply in terms of stressful life events, but also the chronic social stressors that are pervasive in the everyday lives of women.

Third, current life-course research also focuses too much on individual-level factors. It has largely overlooked the lifelong influences of factors at the interpersonal, neighborhood, community, cultural, institutional, and policy levels. Several studies (110, 111) have shown that socioeconomic variations in neighborhoods and communities are associated with differences in pregnancy outcomes, independent of variations in individual socioeconomic characteristics.

However, these studies examined only current neighborhood factors; they did not assess the cumulative effects on birth outcomes of living in segregated neighborhoods or impoverished communities over the life course. Research on disparities needs to move beyond reductionistic comparisons of individual-level risk factors and begin to develop more comprehensive models that examine the influences of multiple factors at multiple levels over the life course.

These limitations point to the need for more integrative research and improved measurements of life-course factors in studying health disparities. In the next section, we will begin to explore a new direction for research. These limitations notwithstanding, we believe that practice and policy also need to move in a new direction to consider women's overall health and development over the life course if we are to eliminate disparities in birth outcomes.

Implications of the Life-Course Perspective for Research, Practice, and Policy

The life-course perspective suggests the need for a more longitudinal and integrative approach toward improving birth outcomes and reducing disparities. We will conclude by considering its implications for research, practice, and policy.

Research

The life-course perspective calls for research that goes beyond comparing exposures to risk and protective factors during pregnancy to comparing cumulative experiences over the life course of the women. As a first step, it calls for better data integration. Databases need to be linked across different stages of pregnancy (preconception/interconception, antepartum, intrapartum, and postpartum) and from one pregnancy to the next. Maternal data need to be linked to not only birth outcomes data, but also data on long-term child health and developmental outcomes. Data also need to be collected and linked at multiple points in a woman's life cycle, and across generations to examine intergenerational effects.

Second, it calls for more longitudinal study designs. Prospective cohort studies with appropriate controls, sufficiently large sample size, oversampling among at-risk populations, and for adequate duration of follow-up are needed. The proposed National Children's Study may provide a platform to begin life-course research around health disparities (112). Pregnant women recruited into the study can be followed prospectively, and their offsprings can be followed from infancy into reproductive years. If the study is continued for a sufficient duration, many of the offsprings may reproduce during the study period, and the health and developmental outcomes of their offsprings can be evaluated with measures collected longitudinally. Such longitudinal study design spanning across three generations will enable researchers to begin to investigate the impact of differential early life programming and cumulative allostatic load over the life course, and perhaps even across generations, on disparities in birth outcomes.

Third, as discussed previously, the life-course perspective calls for an integrative approach to disparities research. As outlined by the National Research Council (113), such approach integrates research across disciplines to investigate health determinants at multiple levels. For example, using an integrative approach, a study on stress and preterm delivery will look beyond perceived stress or stressful life events *during pregnancy* to examine the synergisms among genetic, neuroendocrine, immune-inflammatory, behavioral, psychological, and environmental factors before, during, and in between pregnancies. This will require improved measurements of life-course factors at multiple levels, analytic approaches that better account for longitudinal, multilevel study designs, more sophisticated causal reasoning, and interdisciplinary collaboration among biomedical, behavioral, and social scientists to integrate research on health disparities across multiple disciplines.

Most important, it calls for the creation of an infrastructure to support life-course research. Research priorities need to be defined from the life-course perspective. Grants need to be made on longer funding cycles. Multidisciplinary research network needs to be developed to bridge the existing chasm between biomedical and social–behavioral research on disparities. Long-term community-linked research collaboration needs to be established. Such collaboration can help assure that the science addresses relevant life-course issues in the communities, and that an effective platform to translate scientific research is created. Building community-linked collaboration will be an important first step for doing life-course research on disparities.

Practice

The life-course perspective also calls for clinical and public health interventions that are more

longitudinally and contextually integrated. Instead of being crammed into less than 9 months of prenatal care, such interventions would promote protective factors and mitigate risk factors over a woman's life course. This is what researchers and advocates of women's health have been proposing: healthy women beget healthy children (114, 115). This model highlights the importance of women's health care, of which prenatal care is only one of several components. Equally if not more important is family planning. By preventing unintended pregnancies, family planning might help reduce not only LBW, but possibly also subsequent unemployment and welfare dependency of the mother, developmental delay in the child, and domestic violence and child abuse in the family (116). Also integral to the care continuum are preconceptional, interconceptional, preventive, and primary cares for women. Presently many African American women lack access to this care continuum to a greater extent than to prenatal care. It is our belief that women's health care holds greater promise of improving pregnancy outcomes and eliminating disparities than prenatal care alone, and that the nation will be well served by making a commitment to advance women's health care to a similar extent as it has prenatal care.

But the starting point for women's health is not women's health care. Improving women's health requires access to quality health care not only during their reproductive years, but from womb to tomb. The life-course perspective calls for health care that is longitudinally integrated over women's life span, and it all begins with prenatal care. While the life-course approach suggests that prenatal care may be limited in its effectiveness to reverse the cumulative impact of early life influences and chronic allostatic load on the mother, it recognizes the potential contributions of prenatal care to early programming of the baby's organs and systems, including the reproductive system, for optimal lifelong functioning. Thus the benefits of prenatal care for improving birth outcomes may be more intergenerational than immediate. Rejecting prenatal care on the basis of the lack of demonstrated effectiveness for improving immediate birth outcomes is premature; little is currently known about the possible contributions of prenatal care to health and development over the life course and possibly across generations. Similarly, interventions in early childhood such as Head Start, as well as those during other sensitive developmental periods (e.g., puberty), may also have lifelong impact on women's health (3).

Women's health is the product of not only health care, but multiple factors operating at multiple levels and interacting with each other over the life course of the women. Thus eliminating disparities in birth outcomes will take a more integrative approach that simultaneously addresses these multiple (biological, psychological, behavioral, and social) determinants of women's health (117). Health care providers and public health professionals are not exempt from addressing causes outside of the clinical domain (84, 118). It is imperative that they understand how these multiple factors interact to influence women's health and, consequently, their future pregnancy outcomes. As an example, it has been shown that the typical cost of food is approximately 15–20% higher in poor neighborhoods while the quality of food available is poorer (119). In many disadvantaged communities, there are more liquor stores than grocery stores, and more fast-food restaurants than healthy restaurants (119). For individuals growing up and living in those communities, the relative unavailability of healthy, nutritious food may pattern a lifelong habit of making unhealthy food choices that become difficult to change during pregnancy. Similarly, in many disadvantaged communities, parks and recreation areas are scarce and often unsafe. The relative lack of opportunities (e.g., lack of space, childcare needs, problem with transportation) for physical activities may pattern an inactive lifestyle that often continues into pregnancy. This may also explain why even the most intensive smoking cessation interventions during pregnancy appear to be only modestly effective (120). Most programs do not adequately address the social stressors that underlie the addictive behavior (119). African American women are more likely to grow up and reside in neighborhoods and communities characterized by relative unavailability of healthy food choices, lack of opportunities for physical activities, and more pervasive, chronic social stressors. Prenatal interventions to eliminate racial disparities in birth outcomes are unlikely to be widely effective if they do not address the social contexts of these health behaviors. And waiting until pregnancy begins to change these behaviors may be doing too little too late.

Policy

The life-course perspective has far-reaching policy implications for eliminating disparities in birth outcomes. As a first step, it calls for greater investments

in women's health. Presently many women, particularly low-income women and women of color, lack access to women's health care. Many components of women's health care are not covered or are inadequately covered by public or private insurance (e.g., preconceptional care or primary care for women). Access to continuous health care is limited for many low-income women when they are not pregnant, and they lose their Medicaid coverage at 60 days postpartum even if they had a poor pregnancy outcome. Strategies for expanding coverage include expanding State Children's Health Insurance Program to provide family coverage, enabling Title X to cover preconceptional care, or extending pregnancy-related Medicaid to cover interconceptional care for women with a prior poor pregnancy outcome. Even if coverage is expanded, however, the categorical nature of funding and fragmentation of service delivery for most women's health services impede longitudinal integration of the care continuum. Ultimately a more unified approach toward universal coverage (e.g., universal health insurance) for continuous women's health care is needed. Long-term investments in women's life-course health development will likely yield greater returns on future birth outcomes than will short-term investments in quick fixes during prenatal care.

Second, the life-course perspective calls for greater investments in community health. As long as African American women continue to grow up and reside in neighborhoods and communities that put them at early life disadvantages and under greater cumulative allostatic loads, racial disparities in birth outcomes will likely persist, even with the best pregnancy care or women's health care. This should not be interpreted as a rejection of the contributions that technological advances in pregnancy care have made in improving the health of mothers and infants, but a recognition that eliminating disparities in birth outcomes will take more than simply improving individual-level clinical care (121). It will take building stronger and healthier communities that promote not only healthy pregnancy, but the life-course health development of women and families. While programs that are set up to address community-level factors, such as Healthy Start, have produced mixed results, they seldom have adequate funding to support all the necessary activities of community building (84). Building healthy communities requires investments in infrastructure, such as affordable and decent housing, safe neighborhood, accessible parks and recreation, clean air and water, and competent health care. It also requires community collaborations. What these investments are ought to be decided by and with the community (122). Building healthy communities also requires cross-sectional collaboration (84). No one group or agency can, by itself, address the multiple factors at multiple levels that contribute to health disparities. Maternal and Child Health (MCH) leadership needs to engage MCH and non-MCH partners in a collaborative effort to eliminate disparities in birth outcomes. Such partners may include community police officers to double as outreach workers, municipal transportation authorities to map out more accessible bus routes, and even small convenience store owners to carry healthy groceries. They, too, become "prenatal care providers." Funders need to include in their funding strategies targeted funds for interagency collaborations that would enable a more integrated approach toward improving birth outcomes and eliminating disparities.

Lastly, the life-course perspective calls for greater investments in improving social conditions, with the goal of reducing allostatic load over the life course of women. This requires policymakers to pay attention to issues that disproportionately impact women's lives, such as domestic violence and child care. Men play an important role, positive or negative, in the lives of women and children, and yet they are often treated as an afterthought in MCH. Current policies provide little support, and in some cases, great disincentives, for male involvement in pregnancy and parenting, leaving women to bear greater burdens of childbearing and childrearing. With respect to work, many European countries have produced social legislations (e.g., safeguard of employment, work safety and working conditions, and maternity leave) that have wielded greater protections for pregnant and parenting women than for those in the United States (123). Prolonged working hours, shift work, high stress, low control or reward, inflexibility of work schedule or responsibilities, and gender discrimination can add to the accumulation of allostatic load. For women of color and particularly for African American women, internalized, personally mediated, and institutional racism contribute to further wear and tear on their body's physiologic systems. By improving social conditions, public policy can help eliminate racial disparities in birth outcomes by protecting women, particularly African American women, against the damaging effects of cumulative allostatic load over the life course on their reproductive health.

CONCLUSIONS

In this paper, we proposed an alternative framework for rethinking racial–ethnic disparities in birth outcomes. We contend that such disparities are the consequences of not only differential exposures to protective and risk factors *during pregnancy*, but more important differential developmental trajectories set forth by early life programming and cumulative allostatic load over the life course. It is our hope that this paper will help move future research beyond considering simply pregnancy risk factors to examining the sum of a woman's life experiences. Additionally, we hope that this paper will help move prevailing practice and policy beyond looking for quick fixes during pregnancy to making long-term investments in women's life-course health development. One of the greatest achievements of public health in the last century were the social investments made to improve the overall health of women and communities, which resulted in healthier mothers and babies (124). The health of future generations of mothers and babies will likewise depend upon the strategic long-term investments we make today.

ACKNOWLEDGMENTS

Support for this work was provided by the National Institute of Health Women's Reproductive Health Career Development Fellowship Grant # HD01281-03, and by the federal Maternal and Child Health Bureau for the National Center for Infant and Early Childhood Health Policy Grant # 5U93MC00099.

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